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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,654	06/13/2001	Leanna M. Levine	2842/3	7335

26648 7590 05/17/2005

PHARMACIA CORPORATION  
GLOBAL PATENT DEPARTMENT  
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EXAMINER

WINKLER, ULRIKE

ART UNIT PAPER NUMBER

1648

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/880,654	<b>Applicant(s)</b> LEVINE ET AL.	
	<b>Examiner</b> Ulrike Winkler	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 16 is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11 is/are rejected.
- 7) ☒ Claim(s) 10 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

5.0-0

### DETAILED ACTION

The Amendment filed February 22, 2005 in response to the Office Action of September 20, 2004 is acknowledged and has been entered. Claims 1-11 and 16 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### *Claim Rejections - 35 USC § 103*

The rejection of claims 1-9 and 11 under 35 U.S.C. 103(a) as being obvious over Heath et al. (U.S. Pat. No. 5,235,039, IDS), Bromberg (U.S. Pat. No. 4,203,670) and Maeda (Analytical Biochemistry 1979, IDS) in view of Welch et al. (PNAS 1991, IDS) or Blakeslee et al. (Journal of Immunological Methods, 1976) **is maintained** for reasons of record. Applicants arguments and the Offices response are essential the same as those of record.

Applicants request withdrawal of the rejection because the prior rejection of over Heath et al., Welch et al. and Blakeslee et al. was withdrawn in a prior Office action and Applicant urges that the addition of the Bromberg and Maeda references does not make the instant invention obvious of the cited art. Applicants' argument has not been found persuasive essentially for the reason set forth in the prior Office actions.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of

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ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument based upon the age of the references, contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Applicants' argument is that the Bromberg et al. and the Maeda reference were published 10 years prior to the Heath et al. reference and yet the Heath et al. reference did not use the fluorescence polarimeter in their substrate assay. According to applicants it would therefore not have been obvious to use the Heath et al. substrates in a single well assay. This argument is not convincing for the very simple reason that not all labs are equipped with a fluorescence polarimeters. Heath et al. may have been restricted to the available equipment and had to fashion an assay with those constraints. The order of publication of the references does not have any bearing on whether the combination of references as a whole renders the instant invention an invention non-obvious.

Applicants' additional argument is that the Maeda reference and the Welch et al reference teach the use of full-length protein, which according to applicant are incapable of being bound to a surface. The references citing the full length protein were not used for the purpose of indicating that the full length protein will be bound to a solid surface. It is important to note that neither Maeda or Welch were cited for the proposition of binding the substrate to a solid surface. Welch was cited for the purpose of indicating that certain substrate cleavage sites were already known in the prior art and Maeda et al

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was cited for the purpose of teaching enzyme substrate measurements in a single tube using fluorescence polarization.

Bromberg et al. was cited for the general teaching of how fluorescence polarization works, and for a discussion of what the measurements mean that one obtains using a fluorescence polarimeter. The reference teaches that a decrease in the P value indicates that the molecules are tumbling very fast. The polarizer takes measurements in the parallel and again in the orthogonal direction. If a molecule tumbles fast the same molecule will give a reading in both the parallel and orthogonal directions, this is observed by a decrease in the P value. The Mead et al. reference made use of this principle by taking a large molecule and studying the molecule with the fluorescence compound. As the protease digested the compound this increased the Brownian motion (tumbling) of the protein which in turn decreased the P value. A decrease in P value indicated that the substrate had been digested by the protease. Maeda teaches that the whole protein, i.e. one that is not hydrolyzed by the protease has a larger P value. The shear bulk of the whole protein serves to stabilize the molecule. The Heath et al. reference teaches small substrate compositions that are attached to a solid surface on one side of the scissile bond and the other side of the scissile bond comprises a fluorescein compound. Applicants' argument is that the Bromberg et al. reference and the Maeda reference were published 10 years prior to the Heath et al. reference and yet the Heath et al. reference did not use the fluorescence polarimeter for their substrate assay. According to applicants it would therefore not have been obvious to use the Heath et al. substrates in a single well assay. This argument is not convincing for the very simple reason that not all labs are equipped with a fluorescence polarimeter. Additionally the claims of the

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instant invention uses the transitional term “comprising” which indicated that the methods may employ more steps than those listed in the claim. The substrates taught by Heath et al. and the Maeda substrates are functional equivalents because both substrates achieve a reduction in the tumbling of the substrate molecule. The Heath et al. substrate achieves this by attaching the molecule to a surface, the reference evidences that the substrate is solidly attached to the surface because the reference teaches the additional step of using a filter to remove the liberated fluorescein compound. The Maede reference teaches that the fluorescent substrate when not digest provides a greater P value in the measurements. Therefore, based on what was known to the ordinary artisan at the time the invention was made the substrate taught my Maeda and Heath et al. are functional equivalents of each other.

The instant invention remains rejected as being obvious over Heath et al., Maeda et al. and Bromberg in view of Welch et al. or Blakeslee et al. for the reason set forth above and in the prior Office actions.

### ***Claim Objections***

The objection of claim 10 because of the following informalities **is maintained**:  
The claim is objected to because it depends on a rejected claim. Appropriate correction is required.

### ***Conclusion***

Claim 10 is objected to for depending on a rejected claim.

Claim 16 is allowable.

Claims 1-9 and 11 are rejected.

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

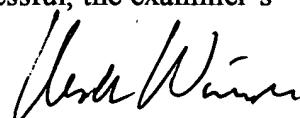
Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.



ULRIKE WINKLER, PH.D.  
PRIMARY EXAMINER

5/12/05